

and the ease of application for multiple lesions is again an advantage here. Keloids were treated with liquid nitrogen when the lesion was of an irregular shape, since greater ease of application was possible than with solid carbon dioxide. The same circumstances prevailed in the choice of liquid nitrogen over solid carbon dioxide in the treatment of certain "strawberry mark" hæmangiomas.

#### ADVANTAGES OF LIQUID NITROGEN THERAPY

The cosmetic result is excellent. Dressings are usually not necessary. Healing is rapid. The material is easily applied to irregular surfaces. The depth of refrigeration is readily controlled. Large warts can be treated without fear of sequelæ. Numerous lesions can be treated at one visit.

#### SUMMARY AND CONCLUSIONS

The practical aspects of the use of liquid nitrogen in the treatment of warts and other skin lesions are noted, and a review of the literature pertaining to cryotherapy in dermatology is presented. The technique of application is described, and our personal experience in the treatment of several hundred verruæ and other skin lesions is related.

Liquid nitrogen was found to be superior to other methods of therapy for verruæ vulgaris which were

either large, multiple or periungual. Liquid nitrogen was found to be a useful adjunct in the treatment of selected cases of leukoplakia, nævus araneus, seborrhœic keratoses, keloids and hæmangiomas.

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#### RÉSUMÉ

On a récemment introduit l'usage d'azote liquide en cryothérapie dermatologique. Ce liquide se tient à une température de  $-195.8^{\circ}$  C. dans des contenants dont l'orifice ne doit pas être hermétiquement fermé afin de permettre l'évaporation. Il est incombustible, inerte, incolore et inodore. On l'applique avec des tampons en badigeonnant la surface de la lésion sans presser jusqu'à ce que la peau blanchisse. L'application provoque une sensation de brûlure suivie pendant quelques heures d'une sensation de piqure. On voit bientôt paraître une phlyctène ou une bulle hémorragique. Le traitement peut être répété aux trois semaines si nécessaire. L'auteur en a fait l'essai dans diverses formes de verrues et plusieurs autres affections de la peau. Cette méthode de traitement produirait une guérison rapide et des résultats cosmétiques excellents.

## Case Reports

### "ACUTE LETHAL CATATONIA" TREATED BY HYPOTHERMIA

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WHEN KRAEPELIN first brought together a wide group of mental illnesses, calling them dementia præcox (subsequently changed by Bleuler to schizophrenia) and dividing them into the hebephrenic, paranoid and catatonic forms, to which Bleuler added a simple form, a great feat of descriptive psychiatry was accomplished and the practice of psychological medicine was accelerated as psychiatrists were able to recognize the features in common between the different groups and apply more specific modes of treatment in each type. Nevertheless, for all that they have in common, in many respects differences between the types continue to outweigh the similarities. This applies

particularly to the natural course of the disease in each type, thus varying the prognosis and response to treatment. The prognosis in the simple and hebephrenic forms is generally considered rather poor, and that in paranoid schizophrenia somewhat better, whereas catatonic schizophrenia has generally speaking the most hopeful outlook of all and in many attacks of this illness a spontaneous and complete resolution may be confidently expected provided the patient can be adequately supported in the meantime.

Despite this generally hopeful prognosis in catatonic schizophrenia, various authors have pointed out that this is not always so, that there is one particular entity whose abrupt downhill clinical course and poor prognosis have earned it the name "acute lethal catatonia". Because this subgroup of the catatonias is at such variance with the remainder, in which the response to conventional methods of treatment is generally rapid and complete, a considerable literature has developed since the original description by Calmeil in 1832 (cited by Aronson and Thompson<sup>1</sup>). Calmeil drew attention to the stormy course of patients with catatonic excitement, passing into profound stupor, with terminal hyperthermia, and then sudden death, though characteristically at autopsy nothing was

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found to explain the hyperthermia and physical collapse that led to death. Patients suffering from severe catatonic schizophrenia may behave with a frenzy of overactivity which would seem to lead to terminal exhaustion and death, or they may pass rapidly into a profound stupor, death taking place after a variable interval in this phase; or the phases may alternate, but in all except the acute lethal catatonias the condition is eventually self-limiting. The exact cause of death in the many patients now reported in the literature with the syndrome of acute lethal catatonia has not been clearly established, but it is significant that in all the accounts death took place via a period of profound stupor passing into a terminal hyperpyrexia. Reports of death at 110° F. appeared in the earliest literature and the highest temperature compatible with survival was 106° F. in the case reported by Aronson and Thompson;<sup>1</sup> they also review the literature up to that time very fully and quote Stenback (1938, 1944 and 1946). No adequate explanation of the hyperpyrexia has so far been brought forward. Gottlieb and Linder<sup>5</sup> concluded that in schizophrenics there seems to be a derangement of central heat-control regulation. This observation has not received the attention that it merits. Rather than an elevated temperature being simply a terminal event, catatonics often have a continuous moderate fever which is assumed by the clinician to be due to overactivity or tonic muscular contraction, dehydration or infection; yet which persists despite correction of these disturbances. It is only as the terminal stage approaches that the temperature ascends to extreme heights and by this time speculation about its origin is abandoned in the face of the imminent death of the patient.

This paper reports a patient suffering from acute lethal catatonia who was treated successfully by hypothermia. It is suggested that hypothermia, as described, is a safe therapeutic procedure which should find application more widely in psychiatry and perhaps largely replace insulin shock and E.C.T.

The patient, Mrs. R., 47 years old and white, was admitted to hospital on March 17, 1959. She had been in her usual state of health until three weeks before; at that time she was noticed to be somewhat withdrawn, quiet and preoccupied but otherwise normal. Her family doctor prescribed some sedation but she continued much the same until nine days before admission. On that occasion a friend found her standing stiffly in a corner of the room, mute and unresponsive. Her doctor advised rest in bed and changed the medication. The patient remained at bed rest for the remaining period of time, taking only very small amounts of nourishment. As she was making no apparent progress and her physical condition was deteriorating, she was admitted to the mental hospital under certification.

She had been married to a man 30 years older than herself; her husband had died approximately eight months before, but the patient did not mourn his loss at the time. She had two children, a boy of 15 and

a girl of four and a half, who was said to be enuretic and a behaviour problem also. The patient had had poliomyelitis at the age of two, which had left her with some permanent weakness of both feet. There were no other illnesses except that five years previously she had an episode somewhat similar to the present illness, at a time when she was living in a remote community. On that occasion she was mute for five days, remaining in bed and refusing food. Her husband would not permit a doctor to be called and the condition resolved spontaneously at the end of the five-day period; she had remained well since. Information about her normal personality indicated that she was an industrious, hard-working woman with little time for leisure or hobbies. Nevertheless, she had many friends in the community where she lived and was always thought of as being a good mother to her children, handling the younger problem child tactfully and firmly.

At the time of admission to hospital, the patient appeared toxic and ill. The admitting doctor noted that she was emaciated and dehydrated with a temperature of 102° F., pulse 106 and respirations 32. Next day (March 18) she was seen by both of us. At that time she was lying in bed, sweating profusely. Physical examination confirmed the bilateral foot drop with flexor plantar responses and wasting of the lower extremities with reduced reflexes. The patient's ill appearance was emphasized by a marked respiratory difficulty; the pharynx was partially filled with mucopurulent secretion which respiration seemed only barely able to pass, and she seemed unable to clear her throat or to swallow. Her mental state was one of almost complete loss of contact except that any attempt to communicate with or examine her caused a shrinking away and aversion, similar to a total withdrawal, in which the patient went into marked flexor spasm, turning away from the examiner and attempting to shut out any stimuli. A determined examination indicated, however, that despite her almost choking on her own sputum, as in the case described by Ferguson,<sup>6</sup> she was perfectly able to cough and clear her pharynx and likewise could swallow small sips with kindly persuasion.

Fluids were administered parenterally to correct the dehydration and antibiotics were given for her respiratory infection which amounted to a tracheo-bronchitis since the lung fields were clear. Over the next three days, despite frequent sponging, approximately five litres of fluid parenterally, and adequate antibiotics, fever persisted, her temperature fluctuating between 101.4° F. and 104° F. Her white blood count was normal at the time of admission, allowing for the dehydration and hæmoconcentration then present, and the blood picture did not vary during the subsequent course in hospital. Repeated examinations did not disclose any explanation for her fever, which was eventually felt to be non-specific and related to her catatonic state more than anything else. Meanwhile, with continued fever, her physical state was progressively worsening and by March 21 (4th day after admission), her condition was fairly critical. At this point it was decided that E.C.T. should be attempted to try to abolish the catatonic process rather than wait any longer for an improvement in her physical condition which was hoped for from the more general methods. The patient was prepared beforehand with a subcutaneous in-

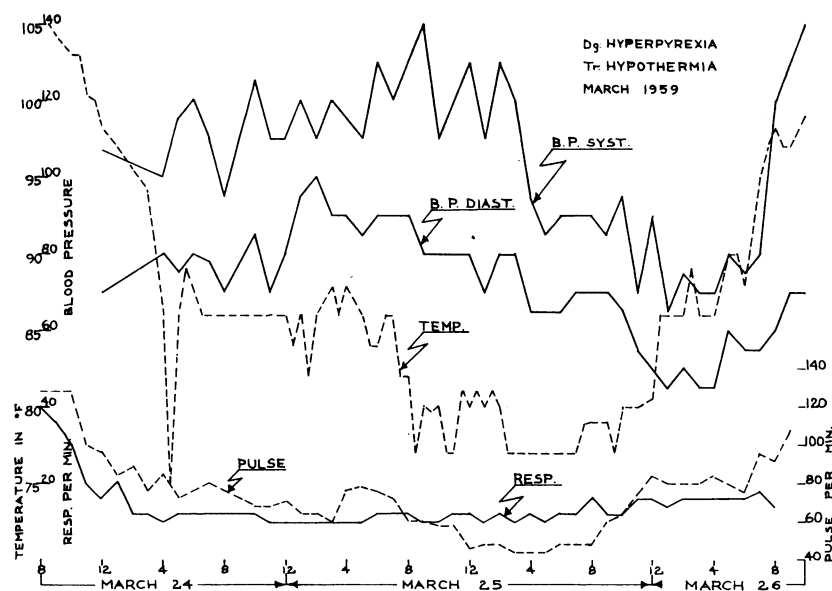


Fig. 1.—Patient's (Mrs. R.) chart. Diagnosis—hyperpyrexia. Treatment—hypothermia, March 1959.

jection of atropine grain 1/75, a Rahm machine was used, and immediately before the current was passed, an intravenous injection of about 15 mg. succinylcholine (Anectine) was given and when relaxation was obtained, a shock of 110 volts for 0.3 sec. was given. As there was no convulsion, the current was increased to 130 volts for 0.4 sec., again with no result. Finally, 130 volts for 0.5 sec. was used and two shocks at this intensity were passed in rapid succession. Again, there was no convulsion and by this time the patient's condition was so poor that it was decided that any further treatment that day was distinctly contraindicated. This contraindication appeared to persist in the succeeding days as her temperature continued to ascend and her general condition deteriorated. On March 22 her temperature was 105° F., pulse 132 and respirations 48 per min.; tepid sponging succeeded in reducing the temperature by one degree Fahrenheit for a brief period only. On March 23 a temperature of 105° F. was recorded and by this time her condition was extremely critical. It seemed that the normal process of heat regulation had ceased and that some central disturbance, of the heat-regulating centre itself perhaps, was forcing up the body temperature to a point where life would no longer be sustained. Later, on March 23, the temperature rose to 106° F. and in the early morning of March 24, 107° F. was recorded despite continuous sponging, electrical fanning and fluid replacement, antibiotics and other measures. By this time, she was mentally completely out of contact; the catatonic features of rigidity previously noted were replaced by an overall flaccidity associated with intermittent muscular fibrillations. At this point, it was decided that abrupt control of the disrupted temperature-regulating mechanism would be the most crucial factor in her survival, and that she must be treated energetically for the effects of heat stroke. One of us (A.G.) proposed the use of hypothermia by Laborit's lytic cocktail technique and it was commenced immediately. Meperidine 50 mg., chlorpromazine 75 mg. and promethazine 50 mg. were given intravenously and ice packs applied to most of the external body surface.

Two hours later her temperature was 100° F. and after an hour and 15 minutes more, was normal at 98.3° F. After this, the temperature continued to drop and a further two hours later it was 94.4° F. Thereafter, it dropped rapidly to 72° F., but this was considered too low in view of the danger of ventricular fibrillation, and the patient's temperature was allowed to stabilize in the region of 80° F. At this level, her pulse was fairly constant at 60 per min. and respirations were eight to ten per min. This state of affairs was maintained for 36 hours. The patient was then rewarmed by removing the ice packing, and the injections of lytic cocktail were spaced farther apart. During the period of refrigeration, the parenteral fluids were maintained and a daily total of 2000 c.c. Code 8

(2/3 of 5% glucose in 1/3 of normal saline) with crystalline insulin 20 units, ascorbic acid 500 mg., hydrocortisone as the sodium succinate ester (Solu-cortef, Upjohn) 100 mg. and calcium gluconate 2 g. was maintained through a venous cannula. In addition, penicillin, two million units intramuscularly, and chloramphenicol, 500 mg. twice daily, were administered throughout. After the cessation of refrigeration, her temperature made a rebound swing to 101° F. for about 18 hours and then subsided spontaneously to normal levels, where it thereafter remained.

Figs. 1 and 2 illustrate the patient's temperature and vital signs during the hypothermia period. Electrolyte levels of the same period are tabulated separately.

During the time the patient was refrigerated, her mental state was one of profound stupor. She would respond to verbal and tactile stimuli but in a non-purposeful manner. Yet the nurses reported she was able to co-operate in nursing procedures from time to time.

On March 27, at a time when her temperature was 101° F., she still appeared to be in a stuporous state in which catatonic negativistic features continued to be present. Thus, there was marked trismus-like clen-

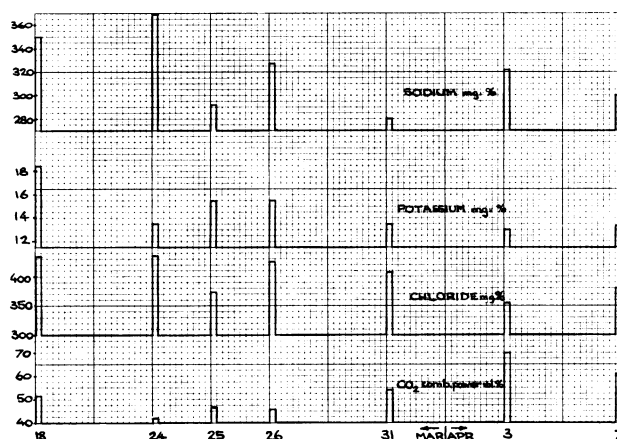


Fig. 2.—Graph showing electrolyte balance.

ing of the jaws on attempts to examine the mouth; resistance to limb movements had returned, although this was by no means as marked as in the period just after admission; and the patient would not communicate with one of us (K.J.F.), although showing at other times, with the nurses, attempts to speak in which she would mutter a few words incoherently. From that time onward, her temperature gradually adjusted to normal levels.

On April 2 she was interviewed at some length by K.J.F. During this examination, she lay in bed and frequently passed into sleep for brief periods. While awake, her level of awareness seemed much impaired and her span of attention was about 10 to 15 seconds. Spontaneous speech was limited to two almost incoherent phrases. Even though awake, the patient appeared to pay sparse attention to questions, except to ask them to be repeated, and thereafter still did not respond. These features were thought to be strong evidence of negativism because immediately after the end of this interview the patient's brother visited, and the patient was observed sitting up partially in bed with mobile facial expression and apparently taking part in the conversation. Later that day, because it was felt that further confirmatory evidence for the diagnosis of catatonic schizophrenia was needed, an intravenous sodium amobarbital test was performed. Approximately 2½ gr. (16 mg.) sodium amobarbital was injected initially and with this quantity the patient passed immediately into an anaesthetized state in which her lower jaw dropped and had to be supported, otherwise respirations would have been completely obstructed. She was quite unrousable and her level of consciousness did not improve until two hours later, by which time she spontaneously awakened. It was felt that this result with intravenous sodium amobarbital was greatly against the diagnosis of catatonic schizophrenia, and a renewed attempt was made to identify a localized lesion of some general process that could be responsible for her illness so far. Neurological examination was negative except for the features already described, noted at the time of admission and due to past poliomyelitis. Spinal fluid examination, E.E.G. and skull radiographs were all normal. A pneumoencephalogram performed successfully on a second attempt was likewise normal. Serum tests for increasing titre of significant viral antibodies were not informative and an insulin tolerance test was within normal limits as well.

Meantime, however, she was showing continued general improvement. Her temperature remained normal and by April 4 the drowsiness previously noted had largely disappeared. This was replaced by apathy and dullness on formal questioning, though she would smile when encouraged. The patient would not perform simple calculations or attempt to answer questions on general information; but she was now aware that she was in hospital, and spent much time examining her hands and arms with an affect of perplexity. By April 8 she had improved markedly in that she was more alert, talkative and friendly than at any time since admission. She could remember visits of friends and relatives during the previous day or two, but had a complete amnesia for the period of her illness stretching back for an indeterminate time into the past. At this time, when told how long she had been in hospital, she would promptly forget. Her mood improved and became at times one of euphoria and foolishness. On

April 11 her attention and concentration amounted to her being able to remember five digits forward and two in reverse, but simple calculations of arithmetical addition involving more than one-digit numbers could not be performed. There was no nominal aphasia, however; no features of right-left disorientation; stereognosis was normal, and no other bedside tests for cortical impairment of function that were performed indicated any definite abnormality.

From this point she continued to make steady general progress. Her brother visited and reported that she now seemed as well as normal, though somewhat tired. The main therapeutic task became one of mobilizing her, first to sit up out of bed and then attempt to walk slowly, but progress was very slow because of the residual poliomyelitis leg-weakness which had become much emphasized by her long period in bed. She was eventually allowed on May 7 to go home and has carried on normally there since.

#### DISCUSSION

Hypothermia as a distinct mode of treatment has an obscure beginning and was probably first used to treat cases of heat stroke occurring in the tropics and in other hot and humid environments, the aim being to secure a decisive lowering of the body temperature for a period of time because part of the syndrome seemed to be due to a paralysis of the heat-regulating centre. Cases have been reported in the literature from time to time in which hyperpyrexia from other causes has been counteracted by hypothermia therapy; typical of the encouraging results obtained is the case mentioned by Matson of Boston: this report is appended to a paper by Reeves and Lewis.<sup>7</sup> In Matson's case, a patient suffered brain-stem contusion, and passed into a state of hyperpyrexia and decerebrate rigidity. Cooling to 90 to 92° F. abolished the rigidity, which would reappear again at 95 to 96° F. Hypothermia was maintained for two weeks and the patient made an excellent recovery from what would apparently have been a fatal condition. In recent years, anaesthetists and surgeons have made extensive use of hypothermia procedures for cardiac and arterial surgery. The advantages are that the basal metabolic rate and oxygen consumption are reduced because of the reduced tissue demand,<sup>8</sup> and patients can survive with a greatly diminished urinary output without a rise in the blood non-protein nitrogen level.<sup>7</sup> However, Knocker experimented with profound hypothermia on dogs and found that significant histological changes took place in various organs, such as fatty infiltration of the liver, adrenals and kidney, and depletion of liver glycogen. She felt that these changes indicated a severe reaction to oxygen deprivation, rather than an intrinsically lessened demand by the tissues themselves; in view of these changes, she reported hypothermia to be a potentially dangerous technique. On the other hand, the changes described are similar to those noted by Selye<sup>9</sup> as part of the alarm reaction, a non-specific effect of stress. In the latter view, in certain types of collagen disease,

the excessive generalized non-specific bodily reaction to stress may bring about more pathological results than the initial external stress itself. This led Laborit<sup>10</sup> to offset the bodily responses to stress in an elective procedure by autonomic blockade; the "lytic cocktail" was compounded of promethazine, chlorpromazine and meperidine. The use of this has enabled hypothermia to be applied more precisely as a technique and this is now standard anaesthetic practice when hypothermia is used. Autonomic blockade abolishes shivering and permits smooth reduction in temperature, balanced maintenance at whatever reduced temperature level is required, and a smooth warming-up period.

Results of psychiatric cases treated with hypothermia have appeared in the literature over the last few years. Opinions of the value of hypothermia range from those of Goldman and Murray,<sup>11</sup> who were "invariably disappointed", to Talbott and Tillotson,<sup>12</sup> who reported "persistent modification of the mental picture". More recently, other authors<sup>13-15</sup> have presented more encouraging opinions. All of these latter groups of workers used hypothermia with autonomic blockade in some form, whereas the poorer opinions of hypothermia seem to have been based on material in which thiopental alone or thiopental and succinylcholine were used and these did not prevent intense shivering,<sup>16</sup> and therefore a stress response. Further, the duration of the hypothermic period showed wide variation in the literature quoted. Hoen, Morello and O'Neill<sup>16</sup> in their personal material quote 3.9 hours below 90° F., whereas Talbott and Tillotson<sup>12</sup> attained 7 hours below 80° F. Another variable that has to be taken into account is the nature of the clinical material used; thus the poorest results have been obtained in patients who have been in hospital for many years whereas in more florid and recent varieties of illness, response to hypothermia has given rise to enthusiastic reports.<sup>13</sup>

In assessing the worth of a new mode of treatment, it is necessary to distinguish the natural course of the illness. In psychiatric conditions, illnesses may, for this purpose, be divided into three categories: first, those in which the clinical course runs spontaneously to complete recovery; second, those which after a variable interval remit and recover but with residual symptoms and deficit of personality; and third, those in which the clinical course is inevitable chronicity or death. An example of the second group is paranoid schizophrenia and examples of the third are hebephrenic schizophrenia, G.P.I. and, as in the case reported by the present authors, acute lethal catatonic schizophrenia. Treatment that works only in the first group of patients is of doubtful validity, treatment that influences progress in group two is probably a valuable addition to the therapeutic range, and treatment effective in the third group is likely to be specific for that condition.

Our patient, Mrs. R., was treated with hypothermia according to the technique of Laborit.

The success of treatment in this otherwise lethal disorder is felt by the authors to have been the result of effective body cooling maintained for a period long enough to counteract thoroughly the disordered inner thermodynamics and permit, at the end of this, a revived heat-regulating centre to recover its normal functions. Stress was effectively avoided and thus the dangers cited by Knocker were averted. As far as we are aware, the temperature levels reached by our patient are the highest recorded compatible with survival in this syndrome. Although the patient suffered a transient Korsakoff syndrome, owing in all likelihood to the sustained hyperpyrexia, she made a good eventual recovery in all respects. We are impressed by the relative ease with which the temperature and general clinical condition can be controlled in what is otherwise, from the nursing point of view, an almost unmanageable condition. Hypothermia by this technique would seem to have an application in a much wider range of psychiatric disorders, especially in those where administration of massive doses of ataractic or sedative drugs, or the use of E.C.T. and insulin shock in a physically poor-risk patient, would previously have been the only alternative treatment.

#### SUMMARY

A case of acute lethal catatonia is described. The literature of this condition and also of the use of hypothermia in psychiatry is reviewed. It is suggested that hypothermia with autonomic blockade should be applied to a wider range of psychiatric disorders, particularly those in which gross behavioural and psychic disturbance would otherwise demand large amounts of medications, dangerous to patients severely debilitated.

We wish to thank Dr. T. G. Caunt, medical superintendent, Provincial Mental Hospital, Essondale, B.C., for kind permission to publish information on this patient under his care, and we acknowledge with deep gratitude the devoted and unremitting nursing attention given throughout by Mrs. M. Bidwell and her nursing staff.

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